Spastic Paraplegia Type 3A

Subjects: Genetics & Heredity

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genetic conditions

1. Introduction

Spastic paraplegia type 3A is one of a group of genetic disorders known as hereditary spastic paraplegias. These disorders are characterized by muscle stiffness (spasticity) and weakness in the lower limbs (paraplegia). Hereditary spastic paraplegias are often divided into two types: pure and complex. The pure types involve only the lower limbs, while the complex types also involve other areas of the body; additional features can include changes in vision, changes in intellectual functioning, difficulty walking, and disturbances in nerve function (neuropathy). Spastic paraplegia type 3A is usually a pure hereditary spastic paraplegia, although a few complex cases have been reported.

In addition to spasticity and weakness, which typically affect both legs equally, people with spastic paraplegia type 3A can also experience progressive muscle wasting (amyotrophy) in the lower limbs, reduced bladder control, an abnormal curvature of the spine (scoliosis), loss of sensation in the feet (peripheral neuropathy), or high arches of the feet (pes cavus). The signs and symptoms of spastic paraplegia type 3A usually appear before the age of 10; the average age of onset is 4 years. In some affected individuals the condition slowly worsens over time, sometimes leading to a need for walking support.

2. Frequency

Spastic paraplegia type 3A belongs to a subgroup of hereditary spastic paraplegias known as autosomal dominant hereditary spastic paraplegia, which has an estimated prevalence of 2 to 9 per 100,000 individuals. Spastic paraplegia type 3A accounts for 10 to 15 percent of all autosomal dominant hereditary spastic paraplegia cases.

3. Causes

Mutations in the *ATL1* gene cause spastic paraplegia type 3A. The *ATL1* gene provides instructions for producing a protein called atlastin-1. Atlastin-1 is produced primarily in the brain and spinal cord (central nervous system), particularly in nerve cells (neurons) that extend down the spinal cord (corticospinal tracts). These neurons send electrical signals that lead to voluntary muscle movement. Atlastin-1 is involved in the growth of specialized

extensions of neurons, called axons, which transmit nerve impulses that signal muscle movement. The protein also likely plays a role in the normal functioning of multiple structures within neurons and in distributing materials within these cells.

ATL1 gene mutations likely lead to a shortage of normal atlastin-1 protein, which impairs the functioning of neurons, including the distribution of materials within these cells. This lack of functional atlastin-1 protein may also restrict the growth of axons. These problems can lead to the abnormal functioning or death of the long neurons of the corticospinal tracts. As a result, the neurons are unable to transmit nerve impulses, particularly to other neurons and muscles in the lower extremities. This impaired nerve function leads to the signs and symptoms of spastic paraplegia type 3A.

3.1 Learn more about the gene associated with Spastic paraplegia type 3A

- ATL1

4. Inheritance

Spastic paraplegia type 3A is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to cause the disorder. In approximately 95 percent of cases, an affected person inherits the mutation from one affected parent.

5. Other Names for This Condition

- spastic paraplegia 3
- spastic paraplegia 3A
- SPG3A

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